

VOMITING AFTER SQUINT SURGERY - NNTs

Nausea and vomiting are unpleasant but common postoperative complications. It is a particular problem for squint correction, because many of these procedures are carried out as day-cases and vomiting can occur as long as 40 hours after operation. In one study of more than 300 outpatients having squint correction, as many as 38% of overnight admissions resulted from vomiting.

Measures which reduced postoperative vomiting, both early and late after operation, would not only benefit the children and their parents, but would also reduce stress on the providers.

Prophylaxis

In these circumstances effective prophylaxis would seem to be a good idea. Is prophylaxis effective?

Some answers come from a systematic review of the prevention of vomiting after paediatric strabismus surgery [1]. Information was available on 2033 children in 27 randomised controlled studies in which drugs from eight different pharmacological classes were used. Because vomiting is an "all-or-nothing" phenomenon, information was available in dichotomous (yes/no) form, allowing calculations of numbers-needed-to-treat (NNT). Vomiting was examined early (up to six hours after operation) and late (up to 48 hours).

Results

Because of the large number of drugs and doses used, there were few treatment groups where sufficiently large numbers of children had been studied to warrant any certainty about results. Ondansetron, for instance, was studied in one trial with 30 patients, though the data for these studies is given in the report [1].

Nevertheless, a number of solid conclusions could be drawn.

Vomiting without active prophylaxis

In the absence of any active prophylaxis (about 400 children in placebo or no-treatment control groups), just over half of the children vomited within six hours. However the range was great; in one trial only 18% of children vomited while in another 88% of children vomited.

Late vomiting (studied in about 300 children) occurred on average in about 60% of children, but again the range in individual trials was wide (43 - 97%).

In these studies children were undergoing the same operation with very similar anaesthetic techniques. Despite this, huge variations in the rate of vomiting occurred. Clearly there are factors other than surgery and anaesthesia which are important (an unknown).

Antiemetics

The best studied antiemetics were droperidol at 75 µg/kg and metoclopramide at 0.15 mg/kg.

NNTs for vomiting and adverse effects for agents used for anaesthesia in squint surgery

Treatment/Outcome	Comparator	NNT (95% CI)
Droperidol 75 µg/kg - preventing early vomiting	Placebo	3.5 (2.8 - 4.8)
Droperidol 75 µg/kg - preventing late vomiting	Placebo	4.4 (3.1 - 7.1)
Metoclopramide 0.15 mg/kg - preventing early vomiting	Placebo	4.0 (2.7 - 7.6)
Metoclopramide 0.15 mg/kg - preventing late vomiting	Placebo	4.1 (2.5 - 12.3)
Propofol - causing oculocardiac reflex	Halogenated anaesthetics	3.6 (1.9 - 4.9)

Droperidol (in about 270 children) was better than placebo in preventing both early and late vomiting, with NNT (with 95% confidence intervals) of 3.5 (2.8 - 4.8) and 4.4 (3.1 - 7.1) respectively. Metoclopramide (in 120 children) produced NNTs for early and late vomiting of 4.0 (2.7 - 7.6) and 4.1 (2.5 - 12.3) respectively.

Minor adverse effects (drowsiness, restlessness, agitation) occurred more frequently with droperidol than in controls with a NNT of 6.3 (4.6 - 10.2). The occurrence of a major adverse effect (extrapyramidal symptoms) was not statistically significant, but had a point NNT estimate of 123.

Propofol

Propofol is an induction agent used intravenously and it has been suggested that its use is associated with a lower incidence of postoperative nausea and vomiting. In a number of studies in which anaesthesia with propofol was compared with anaesthesia without propofol, the incidence of both early and late vomiting was somewhat less, but in the study with the largest numbers the effects barely achieved statistical significance and NNTs were large with wide confidence intervals.

The use of propofol was, however, associated with an incidence of oculocardiac reflex (OCR) of about 50%. This reflex is decrease in heart rate of more than 15-20% which occurs when the eye muscles are pulled during surgery. The bradycardia occurred despite measures to prevent it. The NNT for OCR was 3.6 (2.6 - 6.3); one in every four children given propofol rather than halogenated anaesthetic had a bradycardia.

Comment

There are a number of issues raised by these results. For droperidol 75 µg/kg, four children have to be given the drug to prevent one vomiting; of the other three, one may vomit and two would not have vomited anyway. *Bandolier* 16 examined the issues involved in prophylaxis, including the severity of the medical condition being treated, the effectiveness of the treatment and any adverse effects which might ensue. It is an interesting judgement as to whether prophylaxis is worthwhile here.

This judgement is particularly important when the rate of vomiting without prophylaxis varies so widely. If the incidence of early vomiting in controls (on average 54%) could be brought down to the lowest figure (18%), that would be much more effective than using antiemetic prophylaxis.

The other major point is adverse effects. Perhaps the most important result from this systematic review was that concerning the link between propofol use and OCR. Given that OCR can occasionally become chaotic arrhythmia or sinoatrial arrest, the conclusion that this form of anaesthesia should not be used would seem about right.

That in turn gives purchasers an interesting problem. Just how far into the purchasing system should this be carried. One argument is that the professionals know what they are doing; the contrary is that purchasers are to some extent "in

loco parentis" and should strive to avoid potentially harmful interventions when adequate and safe alternatives exist. Food for thought.

Reference:

M Tramèr, A Moore, H McQuay Prevention of vomiting after paediatric strabismus surgery: a systematic review using the numbers-needed-to-treat method. *British Journal of Anaesthesia* 1995 75: 556-61.

NNTs USED IN DECISION-MAKING IN CHRONIC PAIN MANAGEMENT

Making decisions about the benefits of psychologically-based treatments of medical problems is not easy, and especially difficult to compare with other treatments and to measure relative benefit and cost. Patients whose pain has proved intractable to all reasonable medical and other interventions are chronic consumers of health care - GP or hospital clinic time, analgesic and psychotropic drugs, repeated admissions and sometimes surgery. If rehabilitation treatment enables these patients to carry on more satisfying lives with minimum medical help, how can it be most effectively and economically offered? The use of NNTs may be a start in making decisions of clinical and cost effectiveness.

The study

With a grant from the King's Fund, we compared four-week inpatient treatment (patients looked after themselves in hostel accommodation and went home at weekends) with eight-week half-day outpatient treatment. Pain management methods were taught by the same staff team; they incorporated fitness training, planned increases in activity, activity scheduling, drug reduction, relaxation and cognitive therapy [1,2]. Patients were randomised (dice-throw) to treatment group and controls; there were 41 inpatients, 42 outpatients and 31 waiting list controls.

Outcome measures

Patients listed the treatments they had required for pain before the treatment started, four weeks after the end of treatment and during the year following the end of the intervention - prescribed drugs, a variety of medical and surgical interventions, physiotherapy, acupuncture, osteopathy or chiropractic. A number of physical and psychological measures and drugs taken were also used as outcome measures.

Results

The intention-to-treat analysis (including the 20% who dropped out during treatment or during the period up to the one year to follow up) showed that waiting list controls showed no change, but that treatment both as inpatients and outpatients resulted in benefit.

Benefits of inpatient over outpatient treatment at one year after the end of treatment

Outcome	NNT (95% CI)
Not seeking further medical help over 1 year follow up	4.1 (2.4 - 14.3)
No use of analgesic or psychotropic drug at 1 year	2.8 (1.8 - 6.1)
Walking distance over 10 minutes improved by >50%	5.0 (2.8 - 31.0)
Reduction to non-depressed levels of initially depressed patients	5.6 (not significantly different)

This is good enough, but most interesting was the consistent pattern of NNTs favouring inpatient treatment. At one year after the end of treatment, results favoured inpatient over outpatient treatment, with the NNTs shown in the table.

- For every three patients treated as inpatients rather than outpatients, one patient fewer was taking analgesic or psychotropic drugs.
- For every four patients treated as inpatients rather than outpatients, one patient fewer sought additional medical advice in the year after treatment.
- For every five patients treated as inpatients rather than outpatients, one patient more had a ten-minute walking distance improved by more than 50%.
- For every six patients treated as inpatients rather than outpatients, one patient fewer was depressed.

Comment

The use of NNTs in this complicated area has helped to clarify results without the dubious combination of diverse outcomes. The advantages, both of either treatment over nothing, and of inpatient over outpatient treatment, are consistent. The costs of treatment (£2,000 for each inpatient, £450 for each outpatient) are known. Now drug [3] and medical intervention savings can be estimated and net costs or savings balanced against benefits to patients and carers through improved activity and mood.

While return to work is rare in a group of middle-aged manual or semi-skilled workers, especially those who have had pain for an average of 10 years and have been out of work for little less, there are still benefits not only to the individuals, but also to the community in finding how best to measure their quality of life. NNT may be the key.

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References:

- 1 CE Pither, MK Nicholas. Psychological approaches in chronic pain management. *British Medical Journal* 1991 47:743-61.
- 2 ACdeC Williams. Inpatient management of chronic pain. In M Hodes & S Morley (eds) *Psychological treatment in disease and illness*. London: Gaskell Press (1993).
- 3 CE Pither, JA Ralph. Limiting the drugs list - behavioural treatment not drugs for chronic pain. *British Medical journal* 1993 306: 1687-8.

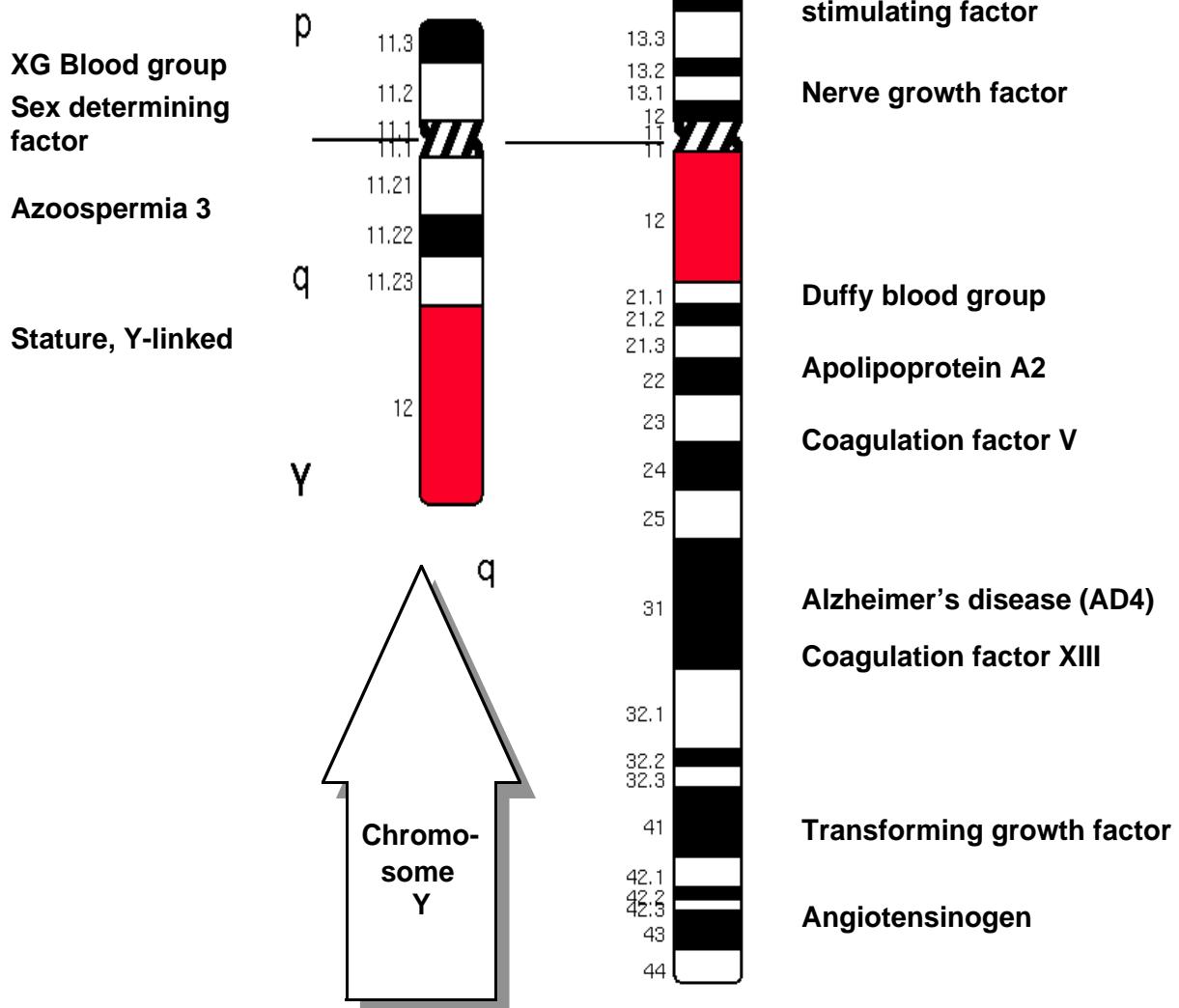
Of p's and q's and chromobabble : introduction to gene maps

Bandolier readers have already been subjected to chromobabble (in *Bandolier* 18). We apologise and offer what we hope is a simple guide to genetic geography, ie human gene maps.

The Human Genome Project will produce the ultimate map the precise ordering and sequencing of the approximately 100,000 genes and 3×10^{-9} base pairs that make up the human genome. Currently (Nov 16th) the OMIM database (see *Bandolier* 21) has 4878 'solid' gene assignments and 2471 'potential or provisional' assignments.

Genetic geography

The first level of mapping is to assign genes to the chromosome regions defined by banding patterns seen after specific staining techniques (such as G banding with giemsa stain). As an example the banding patterns, with bands numbered and some gene assignments are given for chromosomes 1 and Y in the picture. Numbering under the Paris convention is outwards from the chromomere, the short arm is designated p and the long arm q.



What is the significance of this? The point is that we now know where many genes are, we know what some of them do, we know their DNA sequence (sometimes) and most importantly we are beginning to understand how alterations in gene sequences can cause or influence disease.

EVIDENCE-BASED SCREENING

Bandolier has identified a screening blacklist (*Bandolier* 16) highlighting those screening tests on which there is little evidence of cost-effectiveness. What evidence is needed (both clinical and cost effectiveness) before introducing new screening tests? (see also *Bandolier* 19)

Fundamental criteria

The fundamental criteria on which effectiveness of screening should be judged was set out as long ago as 1968 by Wilson and Jungner (WHO Public Health Papers 34). Briefly, a screening test should fulfil ten criteria, including these important points:-

- The condition has a recognisable early phase and early treatment can be shown to improve prognosis.
- Effective treatment is possible and available.
- The test for the condition should be relatively simple, not harmful and acceptable to the patient.
- The test should achieve a balance between false positives and false negatives which is related to the severity of consequences of wrong diagnosis both for the health care system and the patient.
- Screening must be sustainable once introduced and not just part of a limited specific initiative.

Randomised trials

However, even these criteria do not go far enough as we must also ask "Does the test affect the clinical outcome(s) of the disease within a whole population who are at risk?" For example, can screening for aortic aneurysm affect mortality in the community or can screening for *Helicobacter pylori* in primary care improve the detection rate of early gastric cancer?

Invariably the answer to these questions can only be found in lengthy expensive, randomised trials. As the *Bandolier* blacklist highlights, in the current climate it is unlikely that any commissioner would or should accept the introduction of a screening procedure not validated by such trials.

Devil in the details

This, though, is not the end of the story. Randomised trials address clinical outcomes, not whether our health care system can administer a test successfully. Will patients accept the test, what about defaulters and recalls and are all patients at-risk being offered the test? The devil, as always, is in the details. Experience with both breast and cervical cancer screening should warn of the consequences of neglecting these simple questions. To use another example, screening for diabetic retinopathy is unlikely to be effective if a diabetic register has not been compiled and validated regularly.

It is little use waiting for the results of expensive RCTs before introducing screening if more mundane issues about delivery of care are not investigated with equal rigour. Screening can only be effective if *all* those at risk are offered a test and followed up appropriately.

Effective screening is as much a matter of good administration as it is of good medicine. For those contemplating introducing screenings two crucial questions should be answered:-

- Can the proposed test be shown to be cost-effective - *is it worth doing?*
- Can the test be delivered and the results responded to consistently for all those at risk - *can it be done?*

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COMMON CARDIAC CONDITIONS FOR CARD-CARRYING GPs

Dr Nick Hicks for Oxfordshire Health has collaborated with a group of cardiologists, general practitioners and academics to produce brief summaries of the evidence relating to the management of four common cardiac conditions - acute myocardial infarction, chronic atrial fibrillation, chronic heart failure and chronic stable angina. The results of their deliberations are now available on a set of four A3-size plastic cards.

The cards are intended to summarise the clinical trial evidence and carry key messages. They are intended to add to clinical decision making rather than substitute for them.

There is a standard format. The front page carries the topics and main messages - for instance for acute myocardial infarction there are reminders about immediate management, hospital management and post discharge management. The other three pages carry the summarised evidence and its quality estimates of the magnitudes of benefits and risks, some comments and some key references.

These will be useful for GPs particularly. Though most will be familiar with some of the evidence, these cards will not only be useful in developing local, practice or individual guidelines and don't take up much space on the shelf or in the bag.

For more information contact Juliette Gammon, Department of Public Health, Oxfordshire Health, Old Road, Headington Oxford OX3 7LG (Tel 01865 226578). Cards cost £3.50 per set.

CONFERENCE REPORT

An admirably mixed group of enthusiasts including urologists, GPs, public health physicians, nurses, epidemiologists and economists (plus the odd biochemist) enjoyed a lively first *Bandolier* conference in the congenial rural surroundings of Eynsham Hall. Those of you who couldn't get there missed one of the best medical meetings of the year.

Dr Logan Holtgrewe, a recent past chairman of the American Urologists Association, gave clear and entertaining accounts of US practice in BPH and prostate cancer. He emphasised the value of guidelines drawn up for BPH (see *Bandolier* 11) in changing practice for the better.

Other speakers (including Logan's British equivalents) covered the size of the problem in the UK, and existing practice, including the rôle of shared care in the management of patients. The sessions on prostate cancer emphasised the problems of screening, and especially the interpretation of apparently simple PSA results, as well as the wide variation in current practice. The only proposal that met with universal approval was the need for well planned controlled trials which included economic as well as clinical evaluations; the need to wait until better diagnostic tests and treatments are available was a source of some controversy.

A short report of the meeting will be available soon from the *Bandolier* office.

This was an exciting and useful meeting. We have received much useful comment and advice from the participants about what is most useful in getting, evaluating and using evidence. More *Bandolier* conferences are in the planning stage, so watch out for details in the new year.

EVIDENCE-BASED IMPLEMENTATION

In *Bandolier* 18 we carried a simple economic matrix as an aide to decision-making. A more detailed version of this has been developed with Geof McHugh of AEA Technology. It can act as an aid to deciding implementation priorities. *Bandolier* has used this frequently in talks over the last few months, and publishes it here by request.

The matrix balances the health care benefits of, say, a new treatment against the comparative resource use (a much more useful phrase in the health service than cost).

The matrix indicates, for example, that if a new treatment carries significant healthcare benefits (low NN_T when compared with existing treatment) and consumes fewer health service resources, then it should be implemented immediately. Concrete examples might be Helicobacter eradication in peptic ulcer disease, or influenza vaccination in the elderly.

A comparison of two treatments, one of which had more adverse effects at higher cost might well be placed at the other extreme - do not pursue.

Like all such aides-memoir, it will help in some cases but not at others. However as information about clinical and cost-effectiveness is increasingly packaged together in user-friendly lumps (as, for example from the Cochrane Collaboration and the Centre for Reviews and Dissemination), then the chart might just be a useful fixture on the wall above your desk to help in evidence-based priority setting and implementation.

Comparative health care benefits

<i>Higher</i>	<i>Similar</i>	<i>Lower</i>
<i>Higher</i>		
Maybe <i>Prioritised</i> <i>reserve list</i>	Maybe? <i>Put on</i> <i>hold</i>	No <i>Do not</i> <i>pursue</i>
Yes <i>Phased</i> <i>implementation</i>	Maybe <i>Examine</i> <i>further</i>	No <i>Do not</i> <i>pursue</i>
Yes <i>Implement</i> <i>immediately</i>	Yes <i>Manage</i> <i>implementation</i>	Maybe <i>Further analyse</i> <i>benefits & costs</i>

Comparative resource use

Abstracts should carry health warnings

We all manage to try and keep up-to-date with the literature by skimming through the abstracts of papers, and although *Bandolier* seeks to provide help and support for its readers it sometimes has to reveal unpalatable truths that disturb the reader's equanimity.

It is almost 10 years since the proposal for more informative abstracts of clinical articles was published [1]. Yet still many articles do not carry the type of structured abstract recommended by the working group for critical appraisal of medical literature.

An excellent study of "Methodology and overt hidden bias in reports of 196 double-blind trials of non-steroidal anti-inflammatory drugs in rheumatoid arthritis" by Peter Gøetzche published in 1989 [2] reported a number of defects in the trials reviewed. The most worrying statement was that "doubtful or invalid statements were found in 76% of the conclusions or abstracts. Bias consistently favoured the new drug in 81 trials and the control in only one trial."

This message was reinforced by the article about assessing quality of reports [3] which was reviewed in *Bandolier* 17. The additional issue of the need to beware relative risk reduction as a way of presenting information was described in detail in *Bandolier* 21. Rules for abstract reading should therefore be:

- 1 If the abstract is not structured, be very cautious.
- 2 If the abstract of a trial does not describe randomisation, beware.
- 3 If the results are only expressed in terms of 'p' values or relative risk reductions, watch out.

References:

- 1 Ad hoc working group for critical appraisal of medical literature. A proposal for more informative abstracts of clinical articles. *Annals of Internal Medicine* 1987 106: 598-604.
- 2 PC Gøetzche. Methodology and overt and hidden bias in reports of 196 double-blind trials of nonsteroidal anti-inflammatory drugs in rheumatoid arthritis. *Controlled Clinical Trials* 1989 10: 31-56.
- 3 KF Schultz, I Chalmers, DA Grimes, DG Altman. Assessing the quality of randomization from reports of controlled trials published in *Obstetrics and Gynecology* journals. *Journal of the American Medical Association* 1994 272: 125-128.